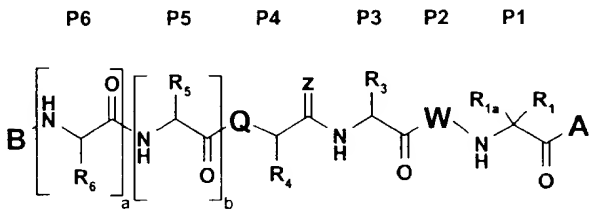
CLEAN COPY OF AMENDED CLAIMS

1. (Four Times Amended) A compound of formula I or a racemate, a diastereoisomer or an optical isomer thereof:



(I)

wherein Q is CH_2 or N-Y wherein Y is H or C_{1-6} alkyl;

a) when Q is CH_2, a is 0, b is 0, and B is an amide derivative of formula $R_{11a}N(R_{11b})$-C(O)- wherein R_{11a} is H; C_{1-10} alkyl; C_6 aryl; C_{7-10} alkylaryl; C_{3-7} cycloalkyl or C_{4-8} (alkylcycloalkyl) optionally substituted with carboxyl; or heterocycle-C_{1-6} alkyl;

and R_{11b} is C_{1-6} alkyl substituted with carboxyl, (C_{1-6} alkoxy)carbonyl or phenylmethoxycarbonyl; or C_{7-16} aralkyl substituted on the aromatic portion with carboxyl, (C_{1-6} alkoxy)carbonyl or phenylmethoxycarbonyl;

or R_{11a} and R_{11b} are joined to form a 3 to 7-membered nitrogen-containing ring optionally substituted with carboxyl or (C_{1-6} alkoxy) carbonyl;

or

b) when Q is N-Y, a is 0 or 1, b is 0 or 1, and

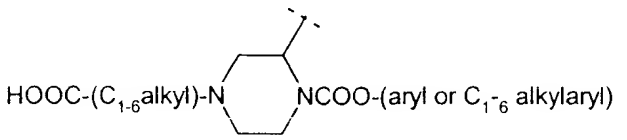
B is an acyl derivative of formula R_{11}-C(O)- or a sulfonyl of formula R_{11}-SO_2 wherein

R_{11} is (i) C_{1-10} alkyl optionally substituted with carboxyl or C_{1-6} alkanoyloxy, C_{1-6} alkoxy, or carboxyl substituted with 1 to 3 C_{1-6} alkyl substituents;

(ii) C_{3-7} cycloalkyl or C_{4-10} alkylcycloalkyl, both optionally substituted with carboxyl, (C_{1-6} alkoxy)carbonyl or phenylmethoxycarbonyl;

(iii) C_6 or C_{10} aryl or C_{7-16} aralkyl optionally substituted with C_{1-6} alkyl, hydroxy, or amino optionally substituted with C_{1-6} alkyl; or

(iv) Het optionally substituted with C_{1-6} alkyl, hydroxy, amino optionally substituted with C_{1-6} alkyl, or amido optionally substituted with C_{1-6} alkyl,



or

,

R_6, when present, is C_{1-6} alkyl substituted with carboxyl;

R_5, when present, is C_{1-6} alkyl optionally substituted with carboxyl;

and

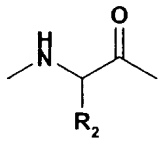
c) when Q is either CH_2 or N-Y, then

R_4 is C_{1-10} alkyl, C_{3-7} cycloalkyl or C_{4-10} (alkylcycloalkyl);

z is oxo or thioxo;

R_3 is C_{1-10} alkyl optionally substituted with carboxyl, C_{3-7} cycloalkyl or C_{4-10} (alkylcycloalkyl);

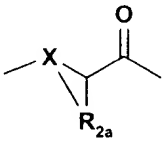
W is a group of formula II:



Formula II

wherein R_2 is C_{1-10} alkyl or C_{3-10} cycloalkyl optionally substituted with carboxyl or an ester or amide thereof; C_6 or C_{10} aryl or C_{7-16} aralkyl; or

W is a group of formula IIa:



Formula IIa

wherein X is CH or N; and

R_{2a} is divalent C_{3-4} alkylene which together with X and the carbon atom to which X and R_{2a} are attached form a 5- or 6-membered ring, said ring optionally substituted with OH; SH; NH_2; carboxyl; R_{12}; CH_2-R_{12}, OR_{12}, $C(O)OR_{12}$, SR_{12}, NHR_{12} or $NR_{12}R_{12a}$;

wherein R_{12} and R_{12a} are independently a saturated or unsaturated C_{3-7} cycloalkyl or C_{4-10} (alkyl cycloalkyl) being optionally mono-, di- or tri-substituted with R_{15},

or R_{12} and R_{12a} is a C_6 or C_{10} aryl or C_{7-16} aralkyl optionally mono-, di- or tri-substituted with R_{15}, or R_{12} and R_{12a} is Het or (lower alkyl)-Het optionally mono-, di- or tri-substituted with R_{15},

wherein each R_{15} is independently C_{1-6} alkyl; C_{1-6} alkoxy; amino optionally mono- or di-substituted with C_{1-6} alkyl; sulfonyl; NO_2; OH; SH; halo; haloalkyl; amido optionally mono-substituted with C_{1-6} alkyl, C_6 or C_{10} aryl, C_{7-16} aralkyl,

Het or (lower alkyl)-Het; carboxyl; carboxy(lower alkyl); C_6 or C_{10} aryl, C_{7-16} aralkyl or Het, said aryl, aralkyl or Het being optionally substituted with R_{16};

wherein R_{16} is C_{1-6} alkyl; C_{1-6} alkoxy; amino optionally mono- or di-substituted with C_{1-6} alkyl; sulfonyl; NO_2; OH; SH; halo; haloalkyl; carboxyl; amide; or (lower alkyl)amide;

or X is CH or N; and R_{2a} is a divalent C_{3-4} alkylene which together with X and the carbon atom to which X and R_{2a} are attached form a 5- or 6-membered ring which in turn is fused with a second 5-, 6- or 7-membered ring to form a bicyclic system wherein the second ring is substituted with OR_{12a}, wherein R_{12a} is C_{7-16} aralkyl;

R_{1a} is hydrogen, and R_1 is the side chain of an amino acid selected from the group consisting of cysteine (Cys), aminobutyric acid (Abu), norvaline (Nva) and allylglycine (AlGly); or

R_{1a} and R_1 together form a 3- to 6-membered ring optionally substituted with R_{14} wherein R_{14} is C_{1-6} alkyl, C_{3-5} cycloalkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, C_6 aryl or C_{7-10} aralkyl all optionally substituted with halo; and

A is hydroxy; or C_{1-6} alkylamino, di(C_{1-6} alkyl)amino or phenyl-C_{1-6} alkylamino;

wherein Het is a five-, six-, or seven-membered saturated or unsaturated, including aromatic, heterocycle containing from one to four heteroatoms selected from nitrogen, oxygen and sulfur, which heterocycle is optionally fused to a benzene ring;

or a non-toxic salt or ester thereof.

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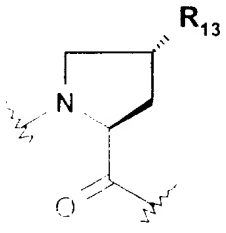
26. (Amended) The compound of formula I according to claim 25, wherein R_{2a} is the side chain of proline substituted with R_{13} at the 4-position with the stereochemistry shown in formula IIIa:



(IIIa)

wherein R_{13} is S-R_{12} or O-R_{12} wherein R_{12} is a C_6 or C_{10} aryl, C_{7-16} aralkyl, Het or -CH_2-Het, all optionally mono-, di- or tri-substituted with R_{15},

wherein R_{15} is C_{1-6} alkyl; C_{1-6} alkoxy; amino; di(lower alkyl)amino; (lower alkyl)amide; C_6 or C_{10} aryl, or Het, said aryl or Het being optionally substituted with R_{16}, and

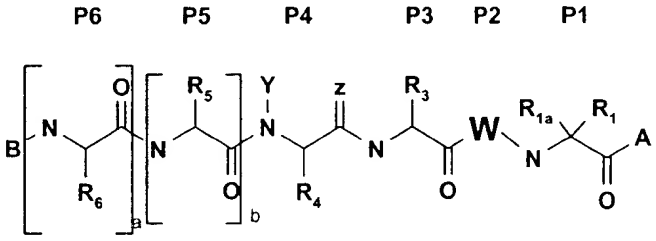
R_{16} is C_{1-6} alkoxy; amino; di(lower alkyl)amino; (lower alkyl)amide; halo; or trifluoromethyl.

E3

30. (Twice Amended) The compound of formula I according to claim 1, wherein R_{1a} is hydrogen and R_1 is the side chain of the amino acid selected from the group consisting of: cysteine (Cys), aminobutyric acid (Abu), norvaline (Nva), and allylglycine (AlGly).

E4

40. (Twice Amended) A compound of formula (IA) or a racemate, a diastereoisomer or an optical isomer thereof:



(IA)

wherein Y is H or C_{1-6} alkyl;

a is 0 or 1;

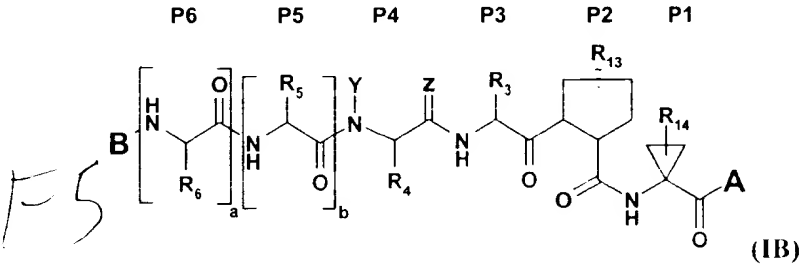
b is 0 or 1;

B is as defined in claim 1, paragraph b);

R_6, R_5, R_4, z, R_3, W, R_1, R_{1a} and A are as defined in claim 1.

E5

45. (Three Times Amended) A compound of formula IB or a diastereoisomer, an optical isomer, a racemic mixture of diastereoisomers or a racemic mixture of optical isomers thereof:



(IB)

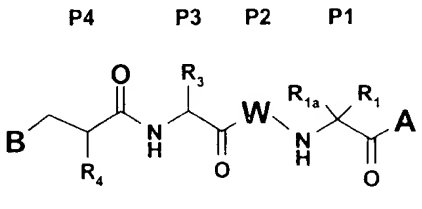
wherein

B, a, b, R_6, R_5, Y, R_4, Z, R_3, and A are as defined in claim 1.

R_{13} is R_{12}, OR_{12}, $C(O)OR_{12}$, SR_{12}, NHR_{12} or $NR_{12}R_{12a}$ wherein R_{12} and R_{12a} are as defined in claim 1; and

R_{14} is C_{1-6} alkyl, C_{2-6} alkenyl optionally substituted with halogen; C_{6-10} aryl or C_{7-10} aralkyl optionally substituted with halogen; or a non-toxic salt or ester thereof.

67. (Twice Amended) A compound of formula IC or a racemate, a diastereoisomer or an optical isomer thereof:

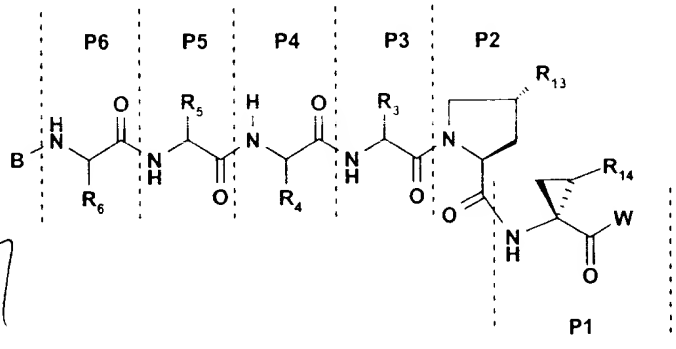


(IC)

wherein B is as defined in claim 1, paragraph a);

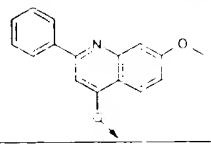
R_4, R_3, W, R_{1a}, R_1, and A are as defined in claim 1.

78. (Amended) A compound of formula (I):



(I)

wherein B, P6, P5, P4, P3, R_{13}, and R_{14} are as defined below, said compound selected from the group consisting of:

Tab 7 Cpd#	B	P6	P5	P4	P3	R_{13}	R_{14}	W
701	Ac	Asp	D-GLU	Ile	Val	OBn	Et	NH-(*S*)-CHMePh
and 702	Dnl	Asp	D-GLU	Chg	Tbg		vinyl	OH

86. (Amended) A tetrapeptide of formula I according to claim 77, selected from the group consisting of compound #: 602; 603; 605; 606; 607; 608; 609; 610; 611; 614; 615; 616; 618;

619; 620; 621; 623; 624; 625; 626; 628; 629; 630; 631; 632; 633; 634 and 635.

Please cancel claims 89-92 without prejudice.

E9 96. (Twice Amended) A composition comprising an anti-hepatitis C virally effective amount of a compound of formula I according to claim 1, or a non-toxic salt or ester thereof, in admixture with a non-toxic carrier medium or auxiliary agent.

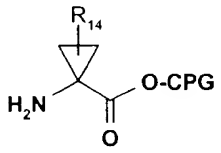
Please cancel claims 97 and 98 without prejudice.

E10 99. (Amended) A combination comprising a compound of formula I according to claim 1, or a non-toxic salt or ester thereof, and an interferon in admixture with a non-toxic carrier medium or auxiliary agent.

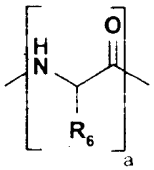
Please add the following new claims 103 to 115:

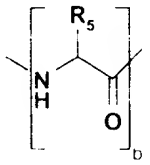
--103. A process for the preparation of a peptide compound of formula (I) according to claim 1, wherein P1 is a substituted aminocyclopropyl carboxylic acid residue, comprising the steps of:

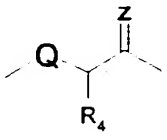
E11 (1) coupling a peptide of the formula: APG-P6-P5-P4-P3-P2-OH with a P1 intermediate of formula:

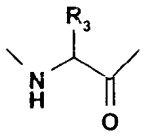


wherein R_{14} is C_{1-6} alkyl or C_{2-6} alkenyl optionally substituted with halogen, APG is an amino protecting group, CPG is a carboxyl protecting group and P6 to P2 are as defined below:

P6: 

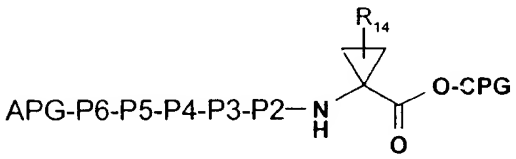
P5: 

P4: 

P3: 

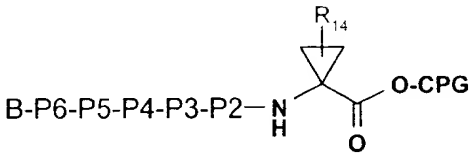
P2: 

wherein W, R_3, R_4, Z, Q, R_5, R_6, a and b are as defined in Claim 1, to obtain a compound of the following formula:



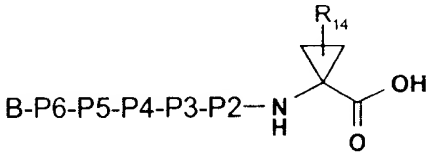
;

(2) cleaving the APG in the compound obtained in step (1) and reacting the resulting unprotected product with a compound of the formula B-Cl wherein B is as defined in claim 1 to obtain a compound of the following formula:



; and

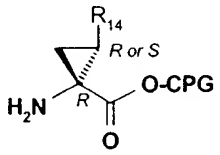
(3) cleaving the CPG in the compound obtained in step (2) to obtain a compound of formula (I) according to claim 1 having the following formula:



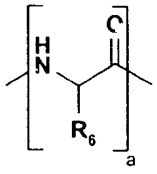
and wherein one or more of the side-chain functionalities in groups P2, P3, P4, P5 and P6 may be protected and deprotected as is necessary during the process.

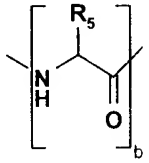
104. A process for the preparation of a peptide compound of formula (I) according to claim 1, wherein P1 is a substituted aminocyclopropyl carboxylic acid residue, comprising the steps of:

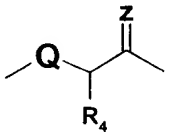
(1) coupling a peptide of the formula: APG-P6-P5-P4-P3-P2-OH with a P1 intermediate of formula:

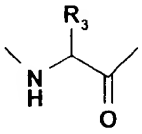


wherein R_{14} is ethyl, vinyl or bromovinyl, APG is an amino protecting group, CPG is a carboxyl protecting group and P6 to P2 are as defined below:

P6: 

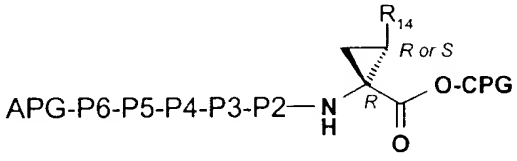
P5: 

P4: 

P3: 

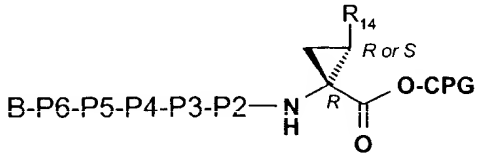
P2: 

wherein W, R_3, R_4, Z, Q, R_5, R_6, a and b are as defined in Claim 1, to obtain a compound of the following formula:



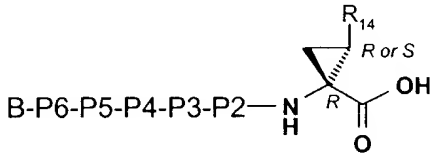
;

(2) cleaving the APG in the compound obtained in step (1) and reacting the resulting unprotected product with a compound of the formula B-Cl wherein B is as defined in claim 1 to obtain a compound of the following formula:



; and

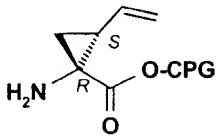
(3) cleaving the CPG in the compound obtained in step (2) to obtain a compound of formula (I) according to claim 1 having the following formula:



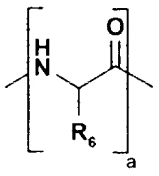
and wherein one or more of the side-chain functionalities in groups P2, P3, P4, P5 and P6 may be protected and deprotected as is necessary during the process.

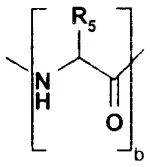
105. A process for the preparation of a peptide compound of formula (I) according to claim 1, wherein P1 is a substituted aminocyclopropyl carboxylic acid residue, comprising the steps of:

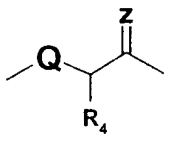
(1) coupling a peptide of the formula: APG-P6-P5-P4-P3-P2-OH with a P1 intermediate of formula:

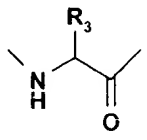


wherein APG is an amino protecting group, CPG is a carboxyl protecting group and P6 to P2 are as defined below:

P6: 

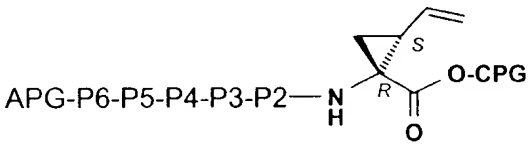
P5: 

P4: 

P3: 

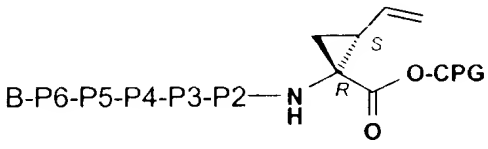
P2: 

wherein W, R_3, R_4, Z, Q, R_5, R_6, a and b are as defined in Claim 1, to obtain a compound of the following formula:



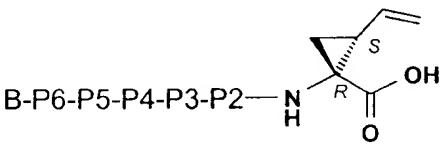
;

(2) cleaving the APG in the compound obtained in step (1) and reacting the resulting unprotected product with a compound of the formula B-Cl wherein B is as defined in claim 1 to obtain a compound of the following formula:



; and

(3) cleaving the CPG in the compound obtained in step (2) to obtain a compound of formula (I) according to claim 1 having the following formula:



and wherein one or more of the side-chain functionalities in groups P2, P3, P4, P5 and P6 may be protected and deprotected as is necessary during the process.

106. The process according to any one of claims 103 to 105 wherein said carboxyl protecting group (CPG) is selected from the group consisting of:
alkyl esters, aralkyl esters, and esters being cleavable by mild base treatment or mild reductive means.

107. A method inhibiting hepatitis C nonstructural protein-3 protease (HCV NS3 protease)

comprising contacting HCV NS3 protease with a compound of claim 1 for a time and under conditions effective to inhibit HCV NS3 protease.

108. A method of inhibiting hepatitis C nonstructural protein-3 protease (HCV NS3 protease) in a cell comprising contacting a cell containing HCV NS3 protease with a compound of claim 1 for a time and under conditions effective to inhibit HCV NS3 protease.

109. A method of inhibiting hepatitis C nonstructural protein-3 protease (HCV NS3 protease) in a mammal infected with hepatitis C virus comprising administering a compound of claim 1 to said mammal for a time and under conditions effective to inhibit HCV NS3 protease.

110. A method of inhibiting hepatitis C nonstructural protein-3 (HCV NS3 protease) in a human infected with hepatitis C virus comprising administering a compound of claim 1 to said human for a time and under conditions effective to inhibit HCV NS3 protease.

111. A method of inhibiting replication of hepatitis C virus comprising contacting hepatitis C virus with a compound of claim 1 for a time and under conditions effective to inhibit hepatitis C nonstructural protein-3 (HCV NS3) protease.

112. A method of inhibiting replication of hepatitis C virus in a mammal infected with hepatitis C virus comprising administering a compound of claim 1 to said mammal for a time and under conditions effective to inhibit hepatitis C nonstructural protein-3 (HCV NS3) protease.

113. A method of inhibiting replication of hepatitis C virus in a human infected with hepatitis C virus comprising administering a compound of claim 1 to said human for a time and under conditions effective to inhibit hepatitis C nonstructural protein-3 (HCV NS3) protease.

114. A combination according to claim 99, further comprising ribavirin.

115. A combination comprising a compound of formula I according to claim 1, or a non-toxic salt or ester thereof, and ribavirin in admixture with a non-toxic carrier medium or auxiliary agent.--